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(19) (CA) **CANADIAN PATENT** (12)

(54) Plasma Phoresis Membrane

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ABSTRACT OF THE DISCLOSURE

A plasmapheresis membrane in the form of hollow threads, tubular foil, or flat foil, produced by a method in which a spinning solution made of cellulose ester is pressed through a spinneret immersed in a precipitation bath, is washed free of solvent with water, is impregnated with a plasticizer-solution, and is dried.

The invention relates to a membrane, more particularly for plasmapheresis, and more especially to a membrane in the form of hollow threads, or fibres, tubular foil or flat foil, made of cellulose esters.

Plasmapheresis membranes are used in plasma separation, that is, the separation of blood plasma from its cellular constituents and the further separation of plasma constituents according to molecular weight.

After plasmapheresis had been carried out for a long time with membrane filters, centrifuges were used for the purpose. In recent times there has been a trend back to filtration processes, one of the reasons for this being that the production of membrane filters has in the meanwhile become more highly mechanized, so that they can now be produced in adequate quantitites at reasonable prices.

U.S. Patent 1,421,341 describes a filter and a production method, the filter being made of a cellulose ester, for example cellulose acetate, which comprises pores suitable for separating bacteria. The filters described may be dried without collapsing the pores.

The filters are produced by pouring a solution of the cellulose ester into a solvent mixture and evaporating the solvent in a moist atmosphere at a low temperature. Enough water is added to the solvent to ensure that the mixture dissolves the cellulose ester. The amount of water governs the size of the pores. The membrane thus obtained is washed in water, is stretched in a wet condition and, after a heat treatment, is dried in hot water or steam.

German Patent 843,088 describes a method for producing ultra filters and diaphragms out of synthetic materials. In this case, porosity is achieved by adding to a plastic

solution, suitable for producing a thin skin, salts soluble therein or other substances, in a solution which is miscible with the plastic solution but does not react therewith, whereupon the mixture is dried, the substance added being dissolved out of the skin thus obtained by means of a solvent which does not dissolve the plastic.

German Auslegeschrift 1,017,596 describes a method whereby a cellulose acetate membrane is produced by the phase inversion process involving pre-gelling in an aerating chamber at an operating temperature of between 20 and 40°C, at a relative atmospheric humidity of between 50 and 70%.

U.S. Patent 2,783,894 describes a similar method for producing a microporous membrane filter from nylon.

German Auslegeschrift 1,156,051 describes a method whereby membranes produced in accordance with the aforementioned U.S. Patents 1,421,341 and 2,783,894 are applied, in a special manner, to a hollow body provided with discontinuities. The pores in the microporous films are less than about 10μm in diameter and comprise, in all, more than 80% of the total volume of the filter material.

German Patent 22 57 697 describes porous cellulose acetate symmetry-membrane filters produced by dissolving cellulose acetate, with a 20-65.5% degree of acetylation, in an organic solvent, the weight ratio being between 5 and 40% of the solvent; and adding a diluting solvent; the boiling point of which is higher than that of the organic solvent; and furthermore adding a metal salt, the metal component of which has an ion radius of less than 1.33 A, is a member of Group I - III of the Periodic System, and has a ratio of between 20 and 200% by weight to the acetate, to the solution, so that a homogeneous solution is obtained.

A thin film of this solution is applied to a flat, polished surface, the solvent therein being removed by evaporation. Microphase separation converts this to a gel. Finally, the metal salts therein are dissolved out in order to form the porous membrane.

The diameter of the pores is between 0.01 and 10μm and porosity is said to be between 70 and 81%.

Under the electron microscope, a 6000 x enlargement of such a membrane reveals a structure which, as seen from the surface, resembles a mat of threads in which threads arranged in loops and emerging at common intersections, lie irregularly above and at the side of each other. As seen in cross-section, the internal structure of the membrane appears as a loose but uniformly dense mass.

German Offenlegungsschrift(Published Patent Specification) 26 06 244 describes a hollow fibre for membrane filtration made from a synthetic or semi synethetic, chain like high polymer which forms threads when spun, the cylindrical wall constituting the hollow fibre comprising, at least in a closed area appearing cross-sectionally as an annular band, a three dimensional, net like structure of fine filter channels having a pore ratio of at least 55% of the active filter area, the active points in the filter channels, which determine the smallest cross sectional dimensions of the channels for the passage of substances contained in a filtration fluid, being distributed at random at least over the active filter zone, and these cross-sectional dimensions being almost uniform. If a membrane of this kind is observed under 3000 to 10,000 x magnification, with an electron microscope, the structure that emerges is reminiscent of a coral colony consisting of a plurality of coral like branched

stems. At the surface of the exterior of the hollow fibre, the branches merge into a grained surface with elongated pore apertures running parallel with each other.

German Offenlegungschrift 28 45 797 describes an anisotropic synthetic membrane having a multi-layer structure, each layer acting as a molecular screen for accurate separation by molecular weight.

Common to all know filter membranes, because of the fixed supporting surfaces used during production, and the at least partial evaporation of the solvent, is a more or less pronounced pore diameter asymmetry. Some filters cannot be stored dry and the pores collapse very easily, even with careful handling. Many known membranes have a wide range of pore diameter distribution, and thus no definite rejection limit. Known methods for producing filter membranes generally operate at moderate speeds, apart from the effects on the membranes produced by production conditions. Recovery of the solvent from air-solvent mixtures is costly, involving heavy losses and environmetnal pollution.

The present invention seeks to produce a filtration membrane in the form of hollow threads, tubular foil or flat foil, with a novel membrane wall structure permitting plasmapheresis filtration to be carried out at high speed, for example, the pore diameter providing a specific rejection limit. Moreover, the disadvantages of known filter membranes are to be eliminated as far as possible.

According to the invention, there is provided a method for producing a membrane, in the form of hollow threads or fibres, tubular foil, or flat foil, made of a cellulose ester which comprises immersing a jet of a spinning solution containing 8 to 25%, by weight, of cellulose ester, 55 to 92%,

by weight, of solvent, and 0 to 20% by weight of at least one additive in a precipitation bath, exposing the jet of solution along a section of the precipitation bath measuring at least 30 cm, at the boundaries of said jet, to the coagulating action of the precipitation bath, removing the coagulated product from said precipitation bath, washing the coagulated product free of solvent with water, impregnating the product with a plasticiser solution, and drying the product.

Suitably the jet of solution is pressed through a spinneret immersed in the bath.

In another aspect of the invention there is provided a membrane, particularly a membrane for plasmapheresis.

The precipitation bath may be made up of liquids, which can be mixed in any proportions with the solvent of the spinning solution, but which do not dissolve or chemically alter the cellulose ester.

A plasticizer may be used, and in particular known plasticizers for cellulose ester, by means of which it can be ensured that the residual water content after drying does not drop below 3 to 15%, by weight, of the weight of the membrane. Polyvalent alcohols and esters have been found particularly satisfactory.

Tubular foils and hollow threads or fibres have been found preferable for membranes used in blood dialysis. They are also preferred for plasmapheresis membranes. In order to obtain a well formed interior with the desired lumen cross-section, membranes in the form of hollow threads or fibres or tubular foil are produced by passing a precipitation bath into the interior of the emerging spinning solution. In this way, the internal boundary of the jet of solution is also exposed to the action of the precipitation bath.

If the composition of the precipitation bath passed into the interior differs from that of the precipitation bath having a coagulating effect upon the external solution-jet boundary, which leads to nonuniform coagulation velocities, this produces varying effects upon the porosity of the internal and external surfaces.

If the precipitation bath contains a large amount of solvent, this results in smaller pores, while a precipitation bath containing a small amount of solvent results in larger pores. However, the concentration of solvent in the precipitation bath should not exceed 20%, by weight. Membranes having satisfactory surfaces properties are obtained when the two precipitation baths are of the same composition.

The membrane according to the invention has a novel cell structure.

The novel membranes of the invention are further illustrated by reference to the accompanying drawings in which:

Figure 1 is an electron microscope photograph of a membrane of the invention in the form of a hollow thread or fibre,

Figure 2 is a photograph showing the pores in greater enlargement, and

Figure 3 is an electron microscope photograph similar to Figure 1 but with greater enlargement.

A cross-section of the wall, even at a 100 x enlargement, reveals a pronounced cell structure reminiscent of a honeycomb, although the boundaries of the close cells are not similar. The cells are approximately rectangular or prismatic, arranged together in rows, and connected smoothly to adjacent cells. The walls of the cells have large numbers

of holes. The pores in the outer walls and cell walls form perforated elements through which the ultra filtrate permeates as is shown in Figure 1.

The composition of the spinning solution is of special significance for the structural properties of the membrane and the purposes for which it may be used, the chemical composition and physical characteristics having complex effects upon the arrangement and dimension of the cells and cell walls.

One factor is the solvent in the spinning solution, for example acetone, dioxane, dioxolan, methyl acetate, nitromethane and methylene chloride.

In general, acetone is preferred. Special preference is given to the use of mixtures of solvents in the spinning solution, because of the wide range of control this gives over the properties and structure of the membrane. A mixture of 50 to 90% by weight of acetone, 5 to 25% by weight of monovalent alcohol, and 5 to 25% by weight of plasticizer has been found particularly satisfactory. The use of monovalent alcohols having 1 to 3 carbon atoms, possibly in admixture with the alcohols, affects the structure in the same way as the amount of plasticizer, glycerine being the preferred plasticizer in the case of membranes to be used for medical purposes. The use of myristyl myristate as the plasticizer in the spinning solution makes it possible to produce structures of interest in industrial applications of the membrane.

The precipitation bath also has a considerable effect upon the properties of the membrane, water with no admixture leading to very large pores, while precipitation baths in the form of aqueous solutions are preferred when

small pores are required. The membranes of the invention may have pores between 0.01 and 50μm in diameter, depending upon the operating conditions selected.

In earlier known plasmapheresis membranes, nitrocellulose was of greater importance than acyl celluloses. Since the handling of nitrocellulose can produce problems, acyl celluloses are now generally more important, and they may be used in the same manner as nitrocellulose for the membranes of the invention. Mixtures of different acyl celluloses may also be processed into membranes of the invention, for example acetyl celluloses, propionyl celluloses and butyryl celluloses. Cellulose acetate is preferred because of its availability.

A filtration membrane formed of pure cellulose triacetate is too hydrophobic for many of the applications of the membrane of the invention. According to one configuration of the invention, the plasmapheresis membrane is made of a cellulose acetate with a substitution degree of between 2.0 and 2.7. The degree of substitution of the cellulose acetate used in the spinning solution also corresponds to the membrane spun therefrom. The degree of substitution preferably amounts to between 2.3 and 2.5.

In the spinning solution, the property having a particular effect upon the structure of the membrane is viscosity. Thus high-viscosity spinning solutions produce membranes with thinner cell walls, which is not detrimental to the mechanical properties if the cell structure is, at the same time, less symmetrical. The viscosity of the spinning solution may be controlled not only by the cellulose ester content, but also by viscosity changing solvents or additives. Solvents containing a group, for example,

isopropanol as a monovalent alcohol, are of higher viscosity than those containing methanol. The viscosity may be lowered, for example, by the addition of halogenated hydrocarbons, for example trichlorotrifluoroethane. The viscosity of the spinning solution is between 5 and 200, preferably between 10 and 100 Pas.

The drying is suitably carried out under temperature conditions such that the average temperature of the material does not exceed 70°C.

In especially advantageous embodiments of the method of the invention, for the purpose of obtaining hollow threads or fibres or tubular foils, a precipitation bath is passed into the interior of the emerging spinning solution. It is desirable for both precipitation baths to be of the same composition.

The solvents used are preferably in the form of mixtures. One preferred mixture consists of 50 to 90%, by weight, of acetone, 5 to 25%, by weight, of monovalent alcohol, and 5 to 25%, by weight, of plasticizer, the monovalent alcohol preferably containing 1 to 3 carbon atoms and the plasticizers being polyvalent alcohols, above all glycerine in medical applications.

The precipitation baths used are in particular, water and aqueous solutions. Among the cellulose esters suitable for the membrane, preference is given in particular to cellulose acetate, especially one with a degree of substitution of between 2.0 and 2.7, more particularly between 2.3 and 2.5. Spinning problems may be largely avoided if the viscosity of the spinning solution is between 5 and 200, preferably between 10 and 100 Pas.

It has been found that a satisfactory production

velocity may be obtained particularly if the jet of solution, after passing along a section of the precipitation bath measuring at least 30 cm, is passed around a deflecting element located after the spinneret, and is removed from the precipitation bath at an angle of between 15 and 60° to the surface of the said bath.

In this connection, it has been found desirable for the spinneret to be immersed into the precipitation bath in such a manner as to form an acute angle with the surface thereof.

The membranes of the invention are noted for their novel structure and are characterized in that each membrane is made out of a closed, stamped, substantially rectangular or prismatic cells, arranged in rows as in a honeycomb, all cell walls being pierced by a plurality of holes in the form of pores.

Generally speaking, the design of the membrane is such that the closed cells are not similar in shape or volume. However, as a result of the production method, there is often a cell wall located approximately symmetrically in the middle of the wall, However, conditions may often be arranged to produce a central cell wall which meanders through the cross-section.

The selectivity of the membrane is affected not only by the pores passing through all of the cell walls, but also by the structure of the cells.

Pigments may, of course, be applied to the membrane in known fashion, if desired.

The invention is illustrated in particular and preferred embodiments in the following examples.

EXAMPLE 1

Production of a spinning solution from cellulose acetate

The following were introduced consecutively into an agitator vessel, the stirring element of which was set to 800 r.p.m.:

3,000 g of methanol

4,000 g of glycerine

2,000 g of cellulose acetate - subst. degree 2.48

11,000 g of acetone

After stirring for two hours at room temperature, the cellulose acetate was dissolved. The solution was then passed through a 20μm mesh filter, was then aerated, and was ready for spinning after 4 to 6 hours. The viscosity of the spinning solution was 15 Pas.

EXAMPLE 2

Production of a membrane according to the invention in hollow thread or fibre form

A gear type metering pump was used to feed 6 ml/min. of the spinning solution, produced as in Example 1, to a hollow thread or fibre spinneret of known design having an outer annular slot 1.300μm in diameter and a slot 150μm in width. The diameter of the central bore forming the cavity was 600μm. The cavity forming liquid consisted of 4.5 ml/min. of sterile water at between 20 and 22°C., which has a coagulating effect as the precipitation bath for the inner boundary of the jet of solution.

The spinneret was immersed into the precipitation bath to a depth of 12 mm, the said bath consisting of sterile water at between 20 and 22°C.

The jet of spinning solution emerging downwardly from the spinneret, after travelling a distance of 60 cm, was deflected around a roller arranged at the bottom of the spinning vat in such a manner as to leave the bath at an angle of 50° to the surface thereof.

In order to remove the remaining solvent, the thread was passed through a water bath for a distance of 120 m. This bath is followed by a plasticizer bath containing a mixture of 92% of water and 8% of glycerine. The hollow fibre was dried in a flow of hot air at between 60 and 70°C. The rate of travel of the thread at the outlet from the installation was 20m/min. The finished hollow thread was made up into a skein of the desired number of threads on a tension controlled drum, was cut to the desired lengths, and processed into filtration units.

The hollow threads thus produced had the following properties:

outside diameter	700 μm
inside diameter	500 μm
tensile strength	78 cN
elongation at rupture	9.1%
pore volume	89.3%
hydraulic permeability	2870 $m/h \cdot m^2 \cdot mmHg$
albumin retention (MW 69000)	2.3% at 0.6 bar
maximal pore width	1.3 μm
inflation or expansion point	1.6 bars

Figure 1 is an electron microscope photograph at 450 x of the cross-section of the plasmapheresis membrane in the form of a hollow thread or fibre according to the

invention, produced by this method. It shows quite clearly the honeycomb cell structure, the walls of the cells appearing dark and the cavities light. Figure 2 shows the pores in 6000 x enlargement. In this case the pores are dark while the wall appears light.

EXAMPLE 3

Production of a plasmapheresis membrane in the form of a tubular foil

A gear type metering pump was used to feed, to an annular slotted nozzle, having an annular diameter of 70 mm and a slot width of 300 mm, 325 ml/min. of the spinning solution described in Example 1. The nozzle was immersed in the precipitation bath to a depth of 10 mm and was arranged vertically, the said bath consisting of sterile water at between 20 and 22°C. A metering pump was used to pump sterile water into the interior of the film of solution emerging in the form of tube. A corresponding amount of this precipitation bath liquid was simultaneously removed from the interior by means of an additional metering pump. The water thus removed contained 50 g/l of acetone. At a distance of 50 cm below the nozzle, the tube thus produced was flattened with a spreader and was passed round a deflecting roller at an angle of 40° to the surface of the bath. After passing through a washing section 72 m in length, in which the tubular foil was washed with sterile water at between 20 and 22°C, the foil was passed through a plasticizer bath 7.20 m in length and was then dried in a channel drier with hot air at between 64 and 74°C. A solution consisting of 8% by weight of glycerine in water was used as the plasticizer bath.

The speed at the outlet from the drier was 9.8 m/min. The following data apply to the tubular foil thus obtained:

width (laid flat)	53 mm
wall thickness	105 μm
tensile strength - longitudinal	102 CN
- transverse	48 CN
elongation at rupture - longitudinal	4.3 %
- transverse	7.1 %
hydraulic permeability	1220 ml/h . m^2 . mmHg.
albumin retention (MW 69000)	4.4 % at 0.6 bar
maximal pore diameter	1.3 μm
inflation or expansion point	1.6 bars

The tubular foil obtained reveals, in cross-section, a relatively symmetrical arrangement of the central cell walls. This structure is particularly suitable for applications requiring optimal filtration and good selectivity.

EXAMPLE 4

Production of a plasmapheresis membrane in the form of a flat foil.

A gear type pump was used to feed 450 ml/min. of the spinning solution described in Example 1 to a wide slotted nozzle 300 mm in width with 270 μm slot width, immersed in the precipitation bath to a depth of 15 mm. The precipitation bath was sterile water at 20°C. The wide slotted nozzle was inclined at an angle of 30° to the direction of travel of the foil. At a distance of 1.40 m below the nozzle, the largely solidified foil was deflected around a roller and passed through the precipitation bath at an angle of 30°. The foil was then passed through a washing section 62 m in length where it was washed with sterile water at between 20 and 22°C. After passing through a plasticizer

bath 6 m in length, containing an 8% by weight solution of glycerine in water, the strip was wiped free of water, passed through an air section 3 m in length, and then to a drier. Using a hot air channel with an air temperature of between 40 and 45°C as a drier, the membranes obtained were as satisfactory as those obtained with a drum drier having surface temperatures between 62 and 72°C. Production velocity at the winding unit was 10.3 m/min.

The following data apply to the flat foil obtained:

width	216 mm
wall thickness	110 μm
tensile strength - longitudinal	82 CN
- transverse	38 CN
elongation at rupture - longitudinal	5.6 %
- transverse	11.2 %
hydraulic permeability	1510 ml/h . m^2 . mmHg
albumin retention (MW 69000)	0.2% at 0.6 bar
maximal pore diameter	1.3 μm
inflation or expansion point	1.6 bars

EXAMPLE 5

Whereas in Examples 2, 3 and 4, it was shown that membranes with the same pore dimensions may be produced as hollow threads, or fibres, tubular foils or flat foils, a description will now be given of how to produce membranes with small diameter pores in the form of hollow threads.

As described in Example 1, a spinning solution of the following composition was prepared:

16.3% by weight of cellulose acetate - subst. degree 2.40

63.3% by weight of acetone

10.2% by weight of methanol

10.2% by weight of glycerine

As in Example 2, 6.9 ml/min. of the spinning solution were fed to the hollow thread spinneret which was immersed, to a depth of 15 mm, in a preciptiation bath consisting of water containing 18 g/l of acetone and 10 g/l of glycerine. 6 ml/min. of a precipitation bath, consisting of 50% by weight of isopropanol and 50% by weight of water, were pumped into the interior of the hollow thread spinneret. After passing through a precipitation bath section measuring 40 cm in length, the jet solution emerging from the nozzle was deflected and left the bath after passing through another section 30 m in length.

The hollow thread thus obtained was washed free of solvent with water, was impregnated with a plasticizer solution consisting of an aqueous glycerine solution with 100 g/l of glycerine, and was then dried in a flow of hot air at 62°C. At the outlet from the installation, the speed of the thread was 20 m/min.

The following data apply to the finished hollow thread:

inside diameter	580 µm
outside diameter	700 µm
tensile strength	174 cN
elongation at rupture	14.7 %
inflation point	10 bars
maximal pore dimension	0.2 µm
hydraulic permeability	372 ml/hm^2 . mmHg
albumin retention	83.3 %

The membrane structure of the hollow thread thus obtained, as seen in cross-section, reveals an asymmetrical arrangement of honeycomb type cells. Membranes of this kind have particularly high tensile strength and elongation at rupture. They are for uses where corresponding mechanical stresses are to be expected.

EXAMPLE 6

It is also possible, according to the invention, to produce membranes having unusually large pores, as indicated hereinafter.

A membrane was produced in the form of a hollow thread, as in Examples 2 and 5. The composition of the spinning solution was as follows:

8.5% by weight of cellulose-acetate subst. degree 2.40
46.5% by weight of acetone
20.0% by weight of methanol
25.0% by weight of glycerine

The precipitation baths consisted of pure water at 20°C. The spinneret was immersed in the precipitation bath at an angle such that the emerging jet solution formed an angle of about 10° with the surface of the bath. After travelling for a distance of 3 m through the precipitation bath, the jet solution was deflected out of the bath. The hollow thread thus obtained was washed free of solvent with water, was treated with a 5.8% glycerine solution, and was dried in a flow of hot air at 70°C. At the outlet from the installation the speed of the thread was 22 m/min.

The following properties were determined:

outside diameter	700 μm
inside diameter	495 μm
tensile strength	32 cN
elongation at rupture	4.2%
hydraulic permeability	4200 ml/h. m^2 . mmHg
inflation point	0.05 bar
maximal pore dimension	40 μm
albumin retention	0

EXAMPLE 7

In this example, a spinning solution is used which, as a result of the inclusion of a viscosity lowering additive, had a viscosity of only 6 Pas with a low cellulose-acetate content. The composition of this spinning solution was as follows:

8.5% by weight of cellulose-acetate
48.5% by weight of acetone
10.0% by weight of methanol
18.0% by weight of glycerine
15.0% by weight of trichlorotrifluoroethane

18 ml/min. of this spinning solution were fed to the hollow thread spinneret described in Example 2. At the same time, 6.6 ml/min. of water were pumped simultaneously into the interior of the emerging jet solution as a cavity forming liquid and as a precipitation bath for the internal boundary of the jet solution. The spinneret was immersed to a depth of 20 mm into the precipitation bath, also consisting of water, for the external boundary of the jet solution. At a distance of 60 cm below the spinneret, the jet solution was deflected and, after leaving the bath, was washed free of solvent with water. After treatment with a 19% glycerine solution, the hollow thread was dried in a flow of air at 62°C.

The following properties were determined:

outside diameter	780 µm
inside diameter	608 µm
tensile strength	90 cN
elongation at rupture	15.6 %
hydraulic permeability	2450 ml/h . m^2 . mmHg
inflation point	0.4 bar
maximal pore dimension	5 µm
albumin retention	2.4 %

Figure 3 shows a 1000 x enlargement of a cross-section of this hollow thread, investigated with a screen electron microscope. It shows a large number of closed cells in slightly asymmetrical arrangement. The differences in cell size are much more pronounced than in the membrane illustrated in Figure 1. As in Figure 2, all external and cell walls are pierced with a plurality of pores.

EXAMPLE 8

Membranes according to the invention having widely varying properties may be produced without difficulty. On the one hand it is possible to make membranes permeable to the whole blood plasma, retaining only the cellular components. On the other hand it is possible to make membranes the rejection limits of which lie at a molecular weight of about 100,000, so that they are permeable to albumin but hold back the other plasma proteins.

A plasmapheresis membrane according to Example 6 was produced in the form of a hollow thread and incorporated into a membrane module having an area of 0.01 m^2.

Another plasmapheresis membrane, having properties similar to those in Example 3, was produced in the form of a hollow thread and incorporated in a membrane module having

an area of 0.01 m^2.

Blood taken from a patient was first passed through the first module at a transmembrane pressure of 100 mmHg at a rate of 3 ml/min., which produced a filtrate I of 0.5 ml/min. The fraction retained contained all of the cellular components. The filtrate was then passed through the second module at a pressure differential of 30 mmHg. The resulting filtrate II contained almost the total albumin, whereas the higher molecular weight protein components remained predominantly in the residue of filtrate I.

Thus the membranes according to the invention permit reinfusion of bodily albumin with the blood cell fraction. This eliminates the need to infuse costly and less compatible foreign albumin.

The patent specifications referred to herein are further identified below:

Federal Republic of Germany Patent 22 57 697, granted September 28, 1978, Kenj Kamide et al, (corresponds to U.S. Patent 3,883,626).

Federal Republic of Germany Offenlegungsschrift 26 06 244, filed February 13, 1976, open to public inspection on August 26, 1976, Mahahiro Mishiro et al (corresponds to U.S. Patents 4,234,431 and 4,340,481.

Federal Republic of Germany Offenlegungsschrift 28 45 797, filed October 20, 1978, open to public inspection on May 3, 1979, Michael Lefebvre et al, (corresponds to U.K. Patent Specification 2,006,643).

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The embodiments of the invention in which an exclusive property or provilege is claimed are defined as follows.

1. A membrane, in the form of hollow filaments or fibres, tubular foil, or flat foil, made of a cellulose ester, which comprises closed cells arranged in rows in the manner of a honeycomb, said cells being substantially rectangular or prismatic, all of the cell walls of said cells being pierced with a plurality of holes forming pore passages, produced by a method in which a spinning solution containing 8 to 25%, by weight, of cellulose ester, 55 to 92%, by weight of a solvent mixture, said mixture comprising 50 to 90%, by weight, of acetone, 5 to 25%, by weight, of monovalent alcohol, and 5 to 25%, by weight, of plasticizer, is immersed as a jet of solution in a precipitation bath, the jet of solution being exposed, along a section of the precipitation bath measuring at least 30 cm, at the boundaries of said jet, to the coagulating action of the precipitation bath, is removed from said precipitation bath, is washed free of solvent with water, is impregnated with a plasticizer solution, and is dried.

2. A membrane according to claim 1, wherein said plasticizer of said spinning solution and of said plasticizer solution is a polyvalent alcohol.

3. A membrane according to claim 2, wherein the polyvalent alcohol is glycerine.

4. A membrane according to claim 1, wherein the cellulose ester is cellulose acetate.

5. A membrane according to claim 4, wherein the cellulose acetate has a degree of substitution of between 2.0 and 2.7.

6. A membrane according to claim 5, wherein the degree of substitution is between 2.3 and 2.5.

7. A method for producing a membrane, in the form of hollow filaments or fibres, tubular foil, or flat foil, made of a cellulose ester, which comprises immersing a jet of a spinning solution containing 8 to 25%, by weight, of cellulose ester, 55 to 92%, by weight, of a solvent mixture, said mixture comprising 50 to 90%, by weight, of acetone, 5 to 25%, by weight, of a monovalent alcohol, and 5 to 25%, by weight, of plasticizer, in a precipitation bath, exposing a jet of solution along a section of the precipitation bath measuring at least 30 cm, at the boundaries of said jet, to the coagulating action of the precipitation bath, removing the coagulated product from said precipitation bath, washing the coagulated product free of solvent with water, impregnating the product with a plasticizer solution, and drying the product.

8. A method according to claim 7, wherein said jet of solution is pressed through a spinneret immersed in said bath.

9. A method according to claim 7, including introducing a precipitation bath into the interior of the emerging spinning solution to produce hollow filaments or fibres or tubular foils.

10. A method according to claim 9, wherein the internal and external precipitation baths are of the same composition.

11. A method according to claim 7, wherein said spinning solution additionally contains up to 20%, by weight, based on the weight of the spinning solution of at least one conventional additive.

12. A method according to claim 11, wherein said additive is selected from the group consisting of pigments and viscosity lowering agents.

13. A method according to claim 7, 8 or 9, wherein the monovalent alcohol has 1 to 3 carbon atoms.

14. A method according to claim 7, wherein said plasticizer of said spinning solution and of said plasticizer solution is a polyvalent alochol.

15. A method according to claim 14, wherein said polyvalent alcohol is glycerine.

16. A method according to claim 7 or 8, wherein said precipitation bath comprises an aqueous solution.

17. A method according to claim 7 or 8, wherein said precipitation bath is water.

18. A method according to claim 7, wherein the cellulose ester is cellulose acetate.

19. A method according to claim 18, wherein the cellulose acetate has a degree of substitution of between 2.0 and 2.7.

20. A method according to claim 19, wherein the degree of substitution is between 2.3 and 2.5.

21. A method according to claim 7, wherein the viscosity of the spinning solution is between 5 and 200 Pas.

22. A method according to claim 21, wherein the viscosity of the spinning solution is between 10 and 100 Pas.

23. A method according to claim 22, including a step of adjusting the viscosity of the spinning solution by including a viscosity controlling additive in the spinning solution.

24. A method according to claim 7, wherein after passing along said section of the precipitation bath measuring at least 30 cm, the jet is passed around a deflecting element, and is removed from the precipitation bath at an angle of between 15 and 60° to the surface of said bath.

25. A method according to claim 24, wherein said jet of solution is pressed through a spinneret immersed in said bath, and said deflecting element is disposed downstream of said spinneret.

26. A method according to claim 25, wherein the spinneret forms an acute angle with the surface of the precipitation bath.

27. A membrane according to claim 1, in the form of a plasmapheresis membrane.

28. A membrane according to claim 1 or 27, formed from a cellulose acetate.

29. A membrane according to claim 1 or 27, wherein said pore passages have a diameter of 0.01 to 50 μm.

30. In a plasmaphoresis device comprising a membrane for separating blood plasma, the improvement wherein said membrane is a membrane as defined in claim 1, 4 or 5.

31. In a plasmaphoresis device comprising a membrane for separating blood plasma, the improvement wherein said membrane is a membrane as defined in claim 7 or 27.

FIG.1.

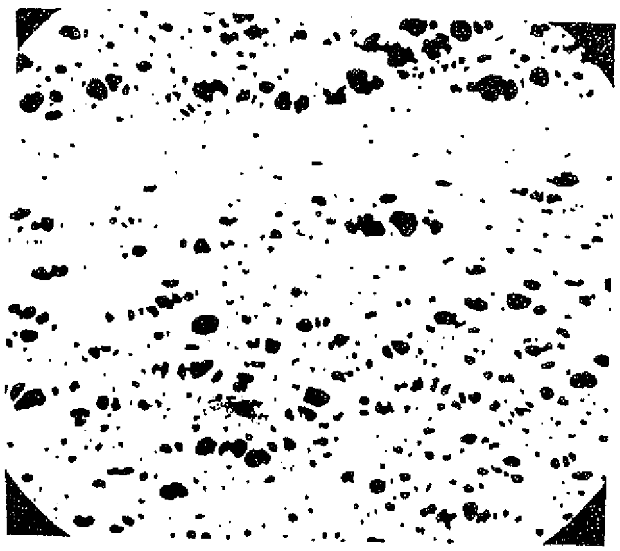

FIG.2.

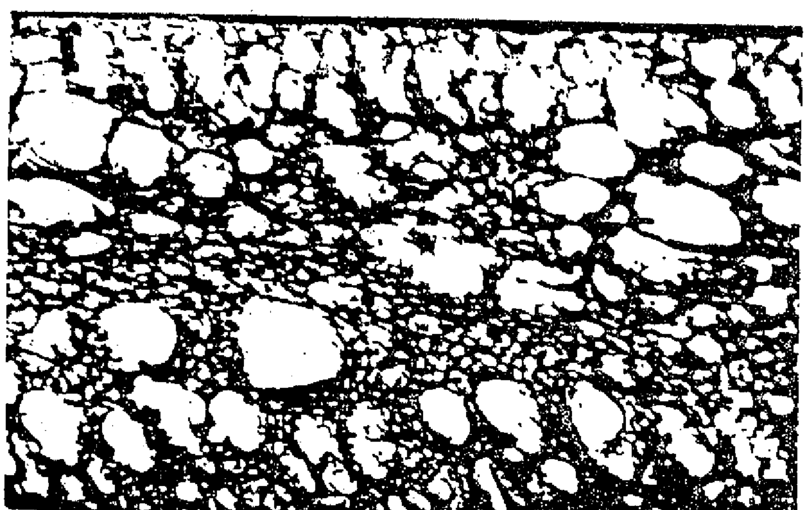

FIG.3.

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